



SEEING THE FUTURE

A REVIEW OF THE ISPE 2016 FACILITY OF THE FUTURE CONFERENCE

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AGENDA

WHAT DOES THE FUTURE LOOK LIKE
CURRENT INDUSTRY STATUS
CURRENT INNOVATIONS
FACILITY OF THE FUTURE CHARACTERISTICS
CASE STUDY – BIOGEN
QUESTIONS & ANSWERS

Facility of the Future Conference

- **November 13-14, 2016 in Bethesda, MD**
- **100 Attendees**
- **Attendees from 11 countries**
- **Speakers from 5 countries**
- **2 FDA speakers**
- **2 Whitehouse speakers**



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What Does the Future Look Like

Vahana by Airbus



What Does the Future Look Like



What Does the Future Look Like



What Does the Future Look Like

The Future of The Pharmaceutical Industry

Competitive and technological changes in the pharmaceutical industry—from powerful new drug chemistries to innovative R&D partnerships and marketing plans—are reshaping the business strategies of many pharmaceutical and biotechnology companies.

According to new research from the MIT Program on the Pharmaceutical Industry (POPI), many companies today are searching for ways to increase productivity, decrease costs, and develop new treatment modalities that will enhance profitability.

These are among the issues we will explore in "The Future of the Pharmaceutical Industry," a one-and-a-half day briefing for senior corporate and technical executives on growth, change and opportunity in the pharmaceutical/biotechnology industry, to be held December 4-5, 1997, in Cambridge, Massachusetts.



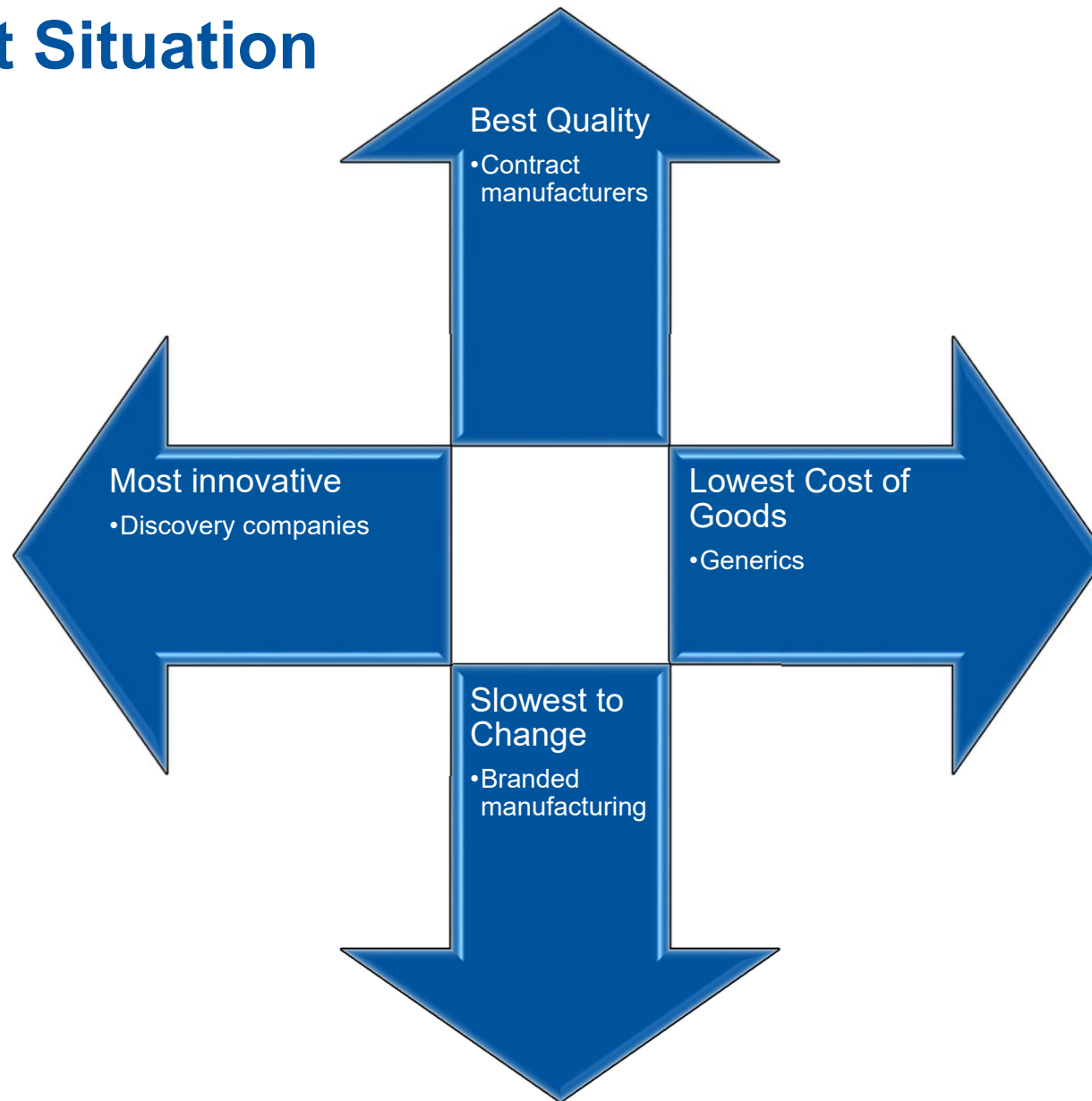
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Current Situation



Industry Trends/Challenges

- **Pressure to reduce high cost of biologics**
 - (\$22/patient day vs \$1/patient day for small molecules)
- **Cost of goods sold: must reduce**
- **Biosimilar to increase large molecule market from current 24%**
- **Orphan drugs are increasing**
- **Complex regulatory environment continues**
- **Innovating in isolation to maintain competitive advantage**
- **Rapid deployment to improve competitive advantage**
- **Skilled workforce shortages**
- **Supply chain challenges**
- **Delivering to global patient population**

Industry Innovations

- **Process analytical tools**
- **Continuous manufacturing**
 - ramp up
 - smaller footprint
 - cost savings
 - avoid tech transfer challenges
- **Single-use systems**
- **Alternative downstream processing techniques**
- **3d Printing – automating biology**
- **Improved controls**
- **Robotic handling**

Factory of the Future - Characteristics

Automation and IT

- **Process metrics**
- **Automation implementation**
- **Data Analytics**
- **Compliance automated**

Life Cycle Operation

- **Change implementation**
- **Low maintenance**
- **Low energy usage**
- **Low environmental impact**

Robust Operation

- **Flexible**
- **Reliable**
- **Resilient to Operator Error**

Design/ Delivery

- **Easy to design, deliver, validate, operate**
- **Continuous processing & real time release**



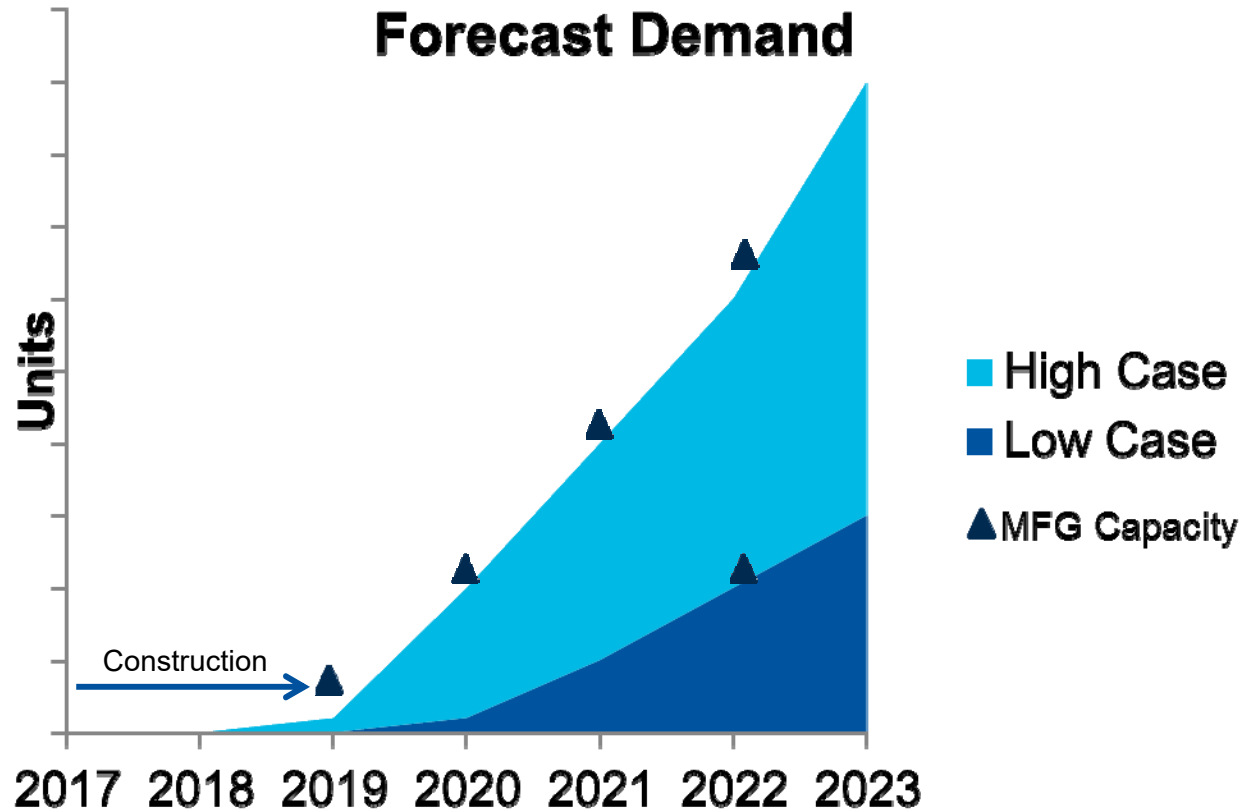
SUPPLYING EXPONENTIAL DEMAND

BIOGEN'S NEXT-GENERATION MANUFACTURING

Phil McDuff
VP, Global Engineering, Biogen
2016 Facilities of the Future
15Nov16

The Challenge:

- Supplying exponential demand



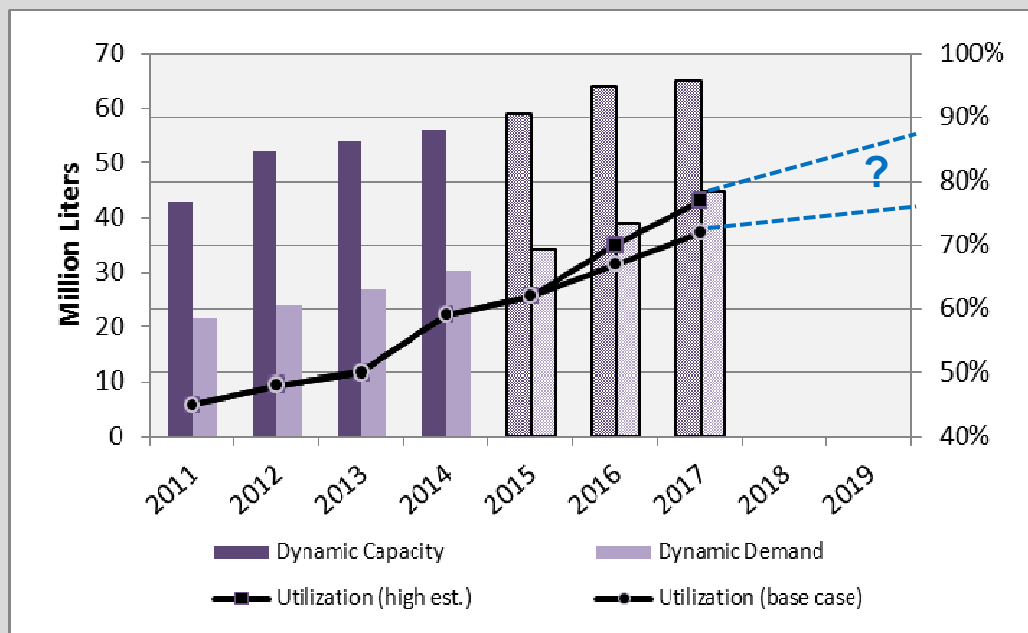
An Industry Challenge

Key Drivers of Biologics Demand Growth³:

- ❖ More products entering Ph2/3 trials
- ❖ Continued growth in oncology
- ❖ Bio-similars / Bio-betters expand market access
- ❖ Growth in predictive personalized drugs

CAGR ³	Capacity	Demand
2007-2012	10%	8%
2012-2017	5%	10%

Manufacturing Capacity Utilization Forecast for Mammalian Cell Culture Industry^{1,3}

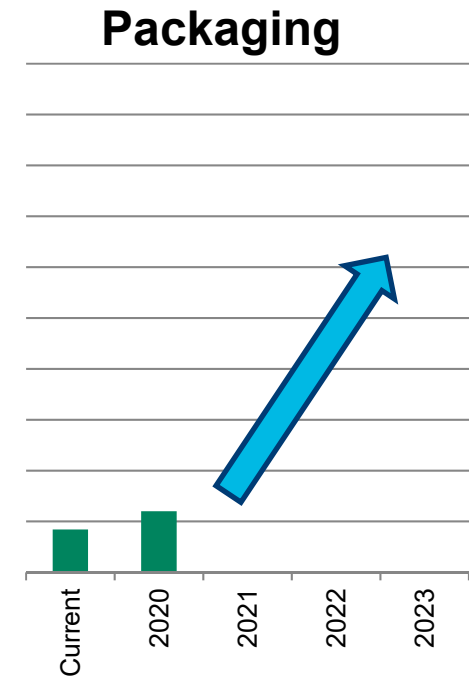
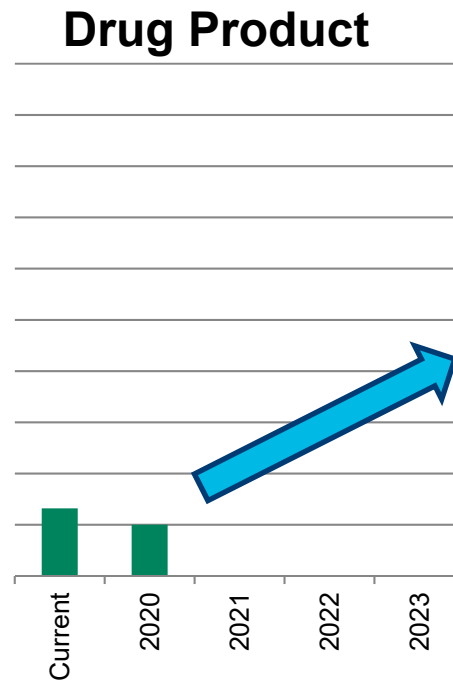
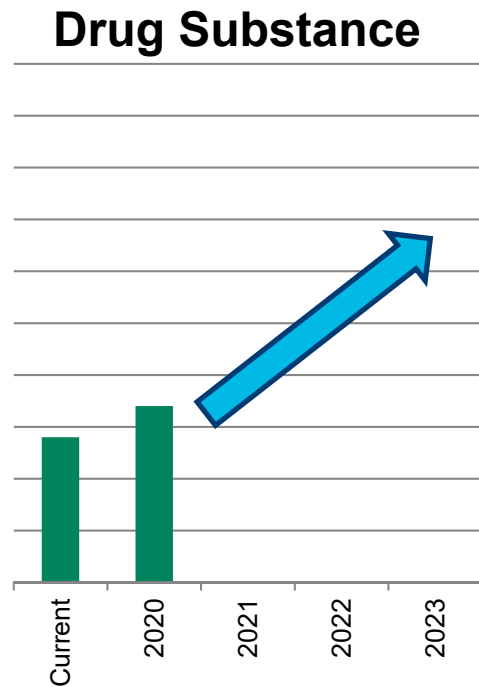


Sources:

1. Ecker, Dawn and Ransohoff, Thomas. *Mammalian Cell Culture Capacity for Biopharmaceutical Manufacturing*, June 2013
2. Skibo, Andrew. *What changes are we seeing in industry and what does that mean for ISPE?* Presentation to ISPE, Annual Meeting 2014
3. Kim, T.H. *Industry Capacity Trends*. Presentation to BioPhorum 2014, 20 May 2014

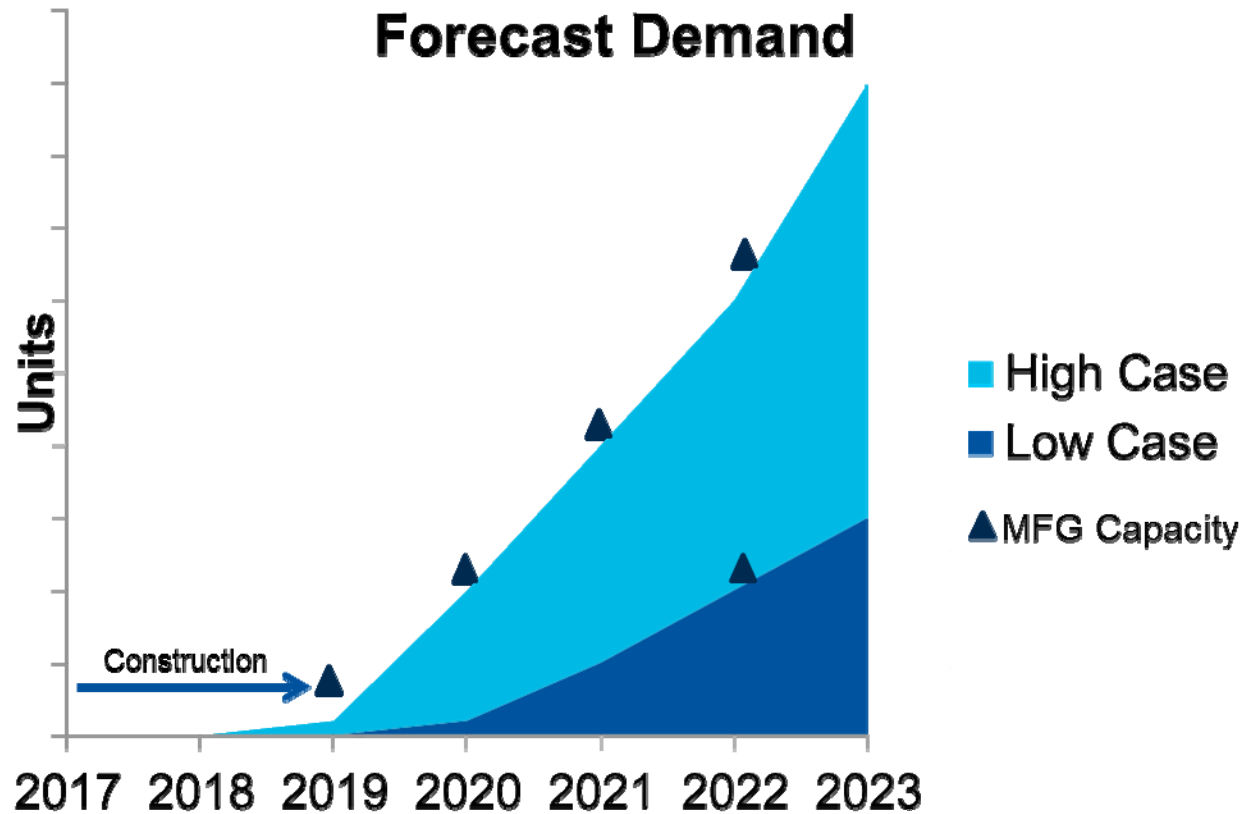
Biogen's Challenge:

Larger Patient Populations



Biogen's Challenge:

- How to prepare for large error bars in DS MFG





Biogen's Next-Generation Manufacturing

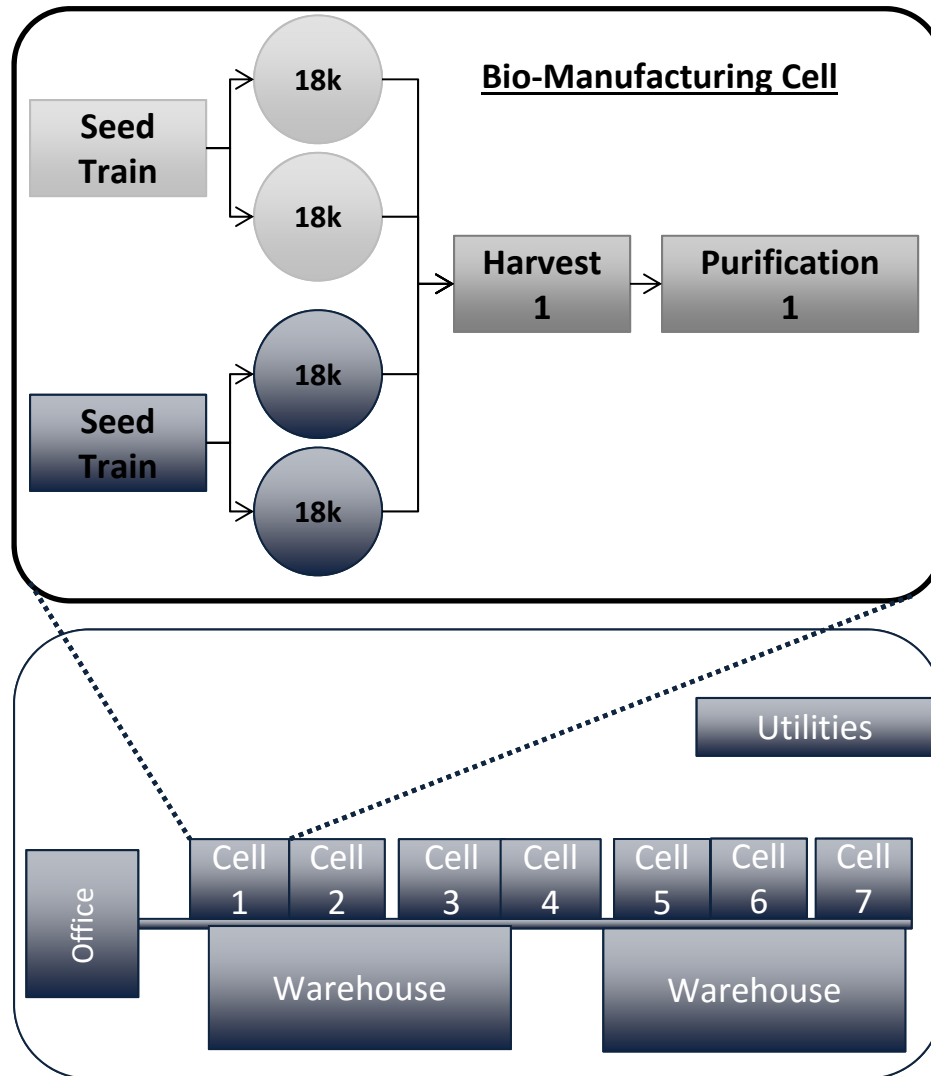


Biogen's Next-Generation Facility

- 10 Metric Ton DS Biologics MFG
- 3X output
- New MFG Platform
- Bio-Manufacturing Cell (BMC) Design
- Next-Gen Operations
- Integrated Execution Systems



BMC Concept



BIOGEN'S TEN METRIC TON ANTIBODY PRODUCTION CELL

- Modular design
- Optimized for throughput
- Build capacity in units of production cells; allows for faster delivery post initial investment
 - 44 months from groundbreaking to first cell
 - Additional cells in 24 months
- Each cell designed for up to **15 g/L**
- Initial scope: two production cells, utility building, warehouse, lab/office space

Site Master Plan

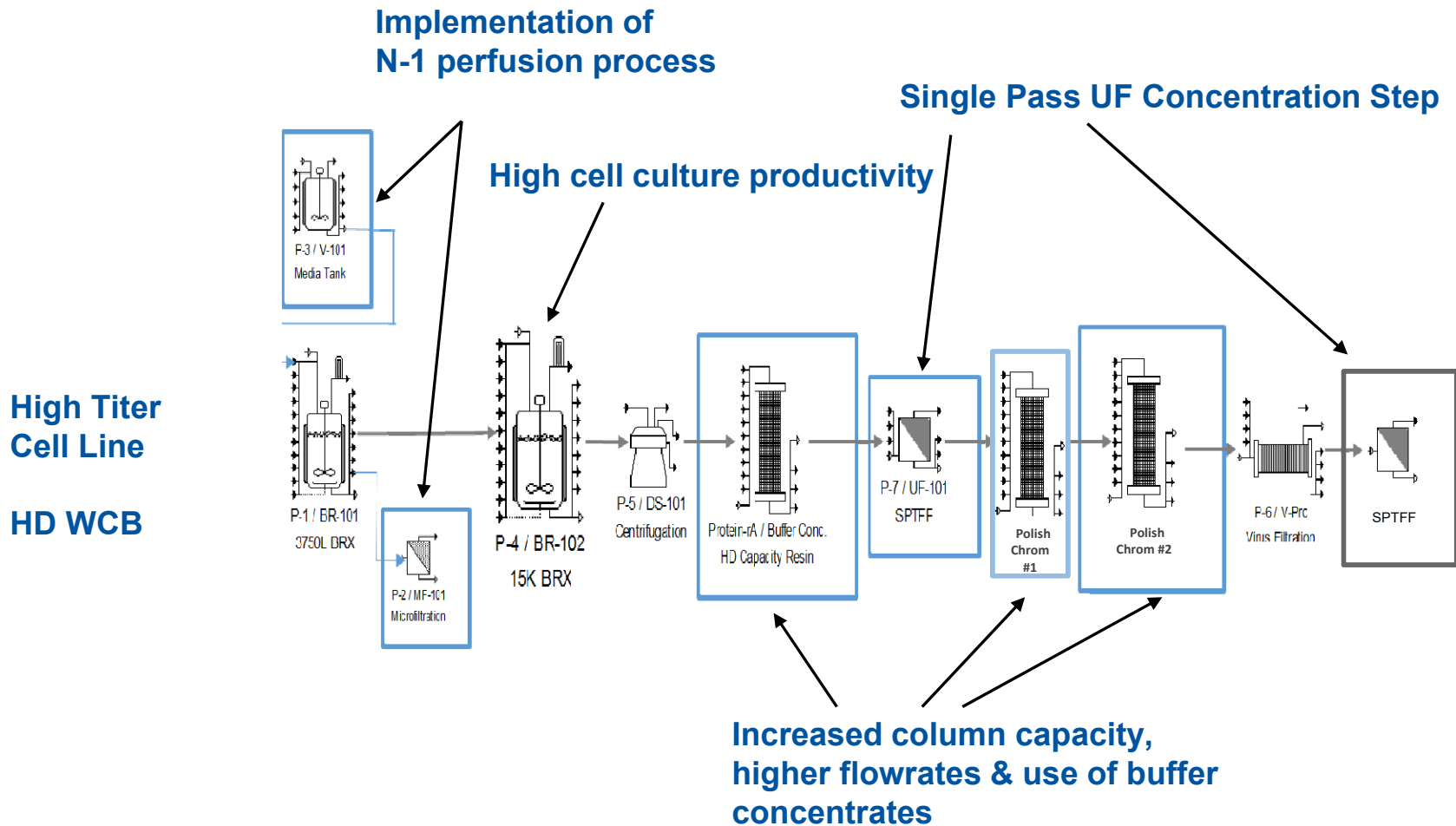


Advanced Process Design Concepts



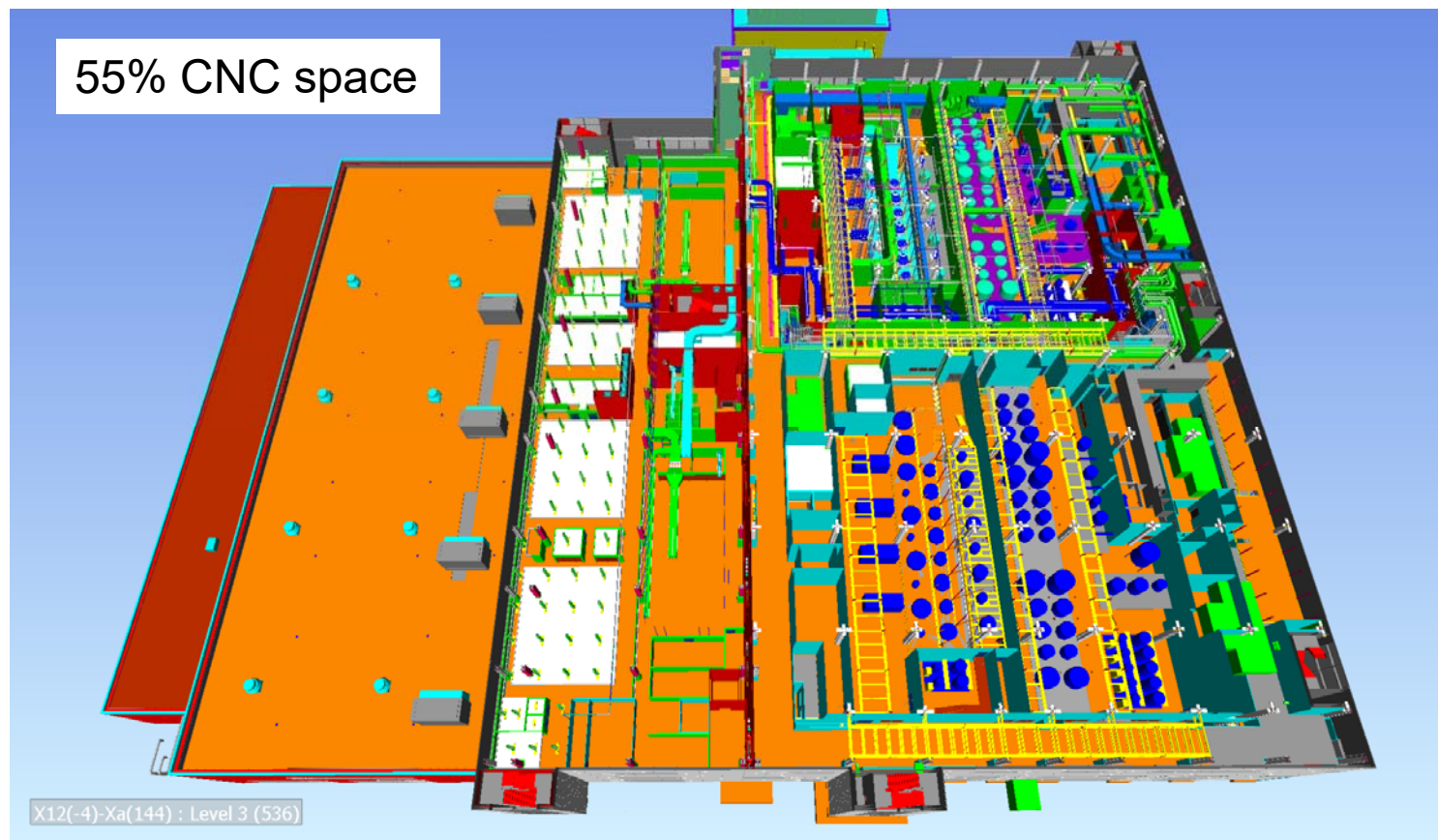
- Perfusion N-1 Bioreactor
- Continuous Discharge Centrifuge
- High Capacity Resins
- Buffer Concentrates
- SPTFF Concentration
- Closed System application
- Supply Loops for Caustic and Glucose

Improved Process – 3X Output



Closed Systems Processing

Broad use of closed systems through Seed Train and Production Bioreactor areas reduces classified space



Reduce Preps - Supply Loops

Glucose projection ~10,000 liters/batch.

- > 20 Totes moved through the facility
- Inc costs for HTST material

Caustic projection ~15,000 liters/batch

- ~ 10 preps/batch
- ~ 5 IBCs and ~ 5 containers/batch

Hot and Ambient WFI Loops

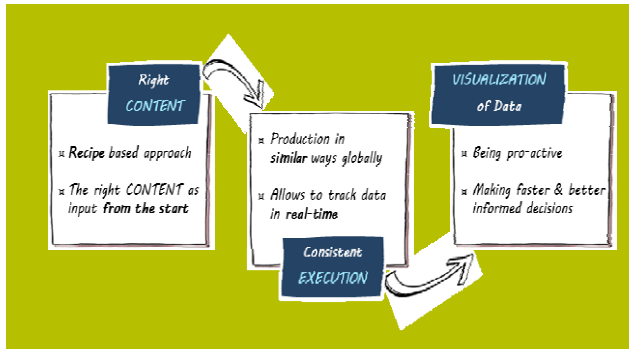
- Reduce water usage and cooling time

Guiding Principles for Operations



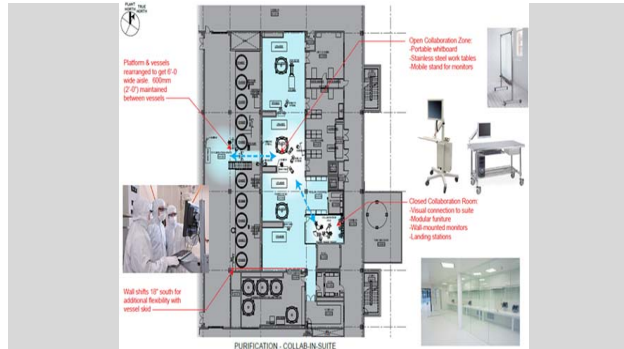
- Science drives decisions
- Technology enables systems
- Integrated is the way we work

High Performance Operations



Highly Automated & Integrated

- Full recipe operation
- End to End Visibility
- Execution systems implemented according to industry standards



Decisions are made on the floor

- Visual work place allowing use of KPI & process data
- Office areas & labs integrated into manufacturing
- Multivariate predictive modeling

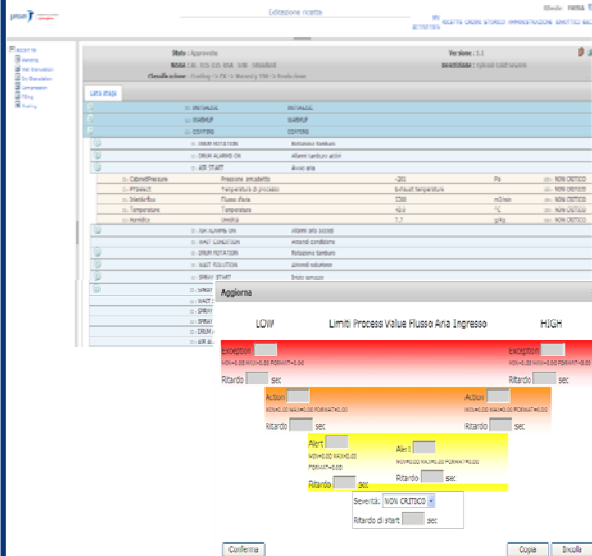


Right Time Release

- Localized testing
- Exception based batch disposition
- Data immediately available for regulatory filing

Enabling Content /Execution /Visualization Framework

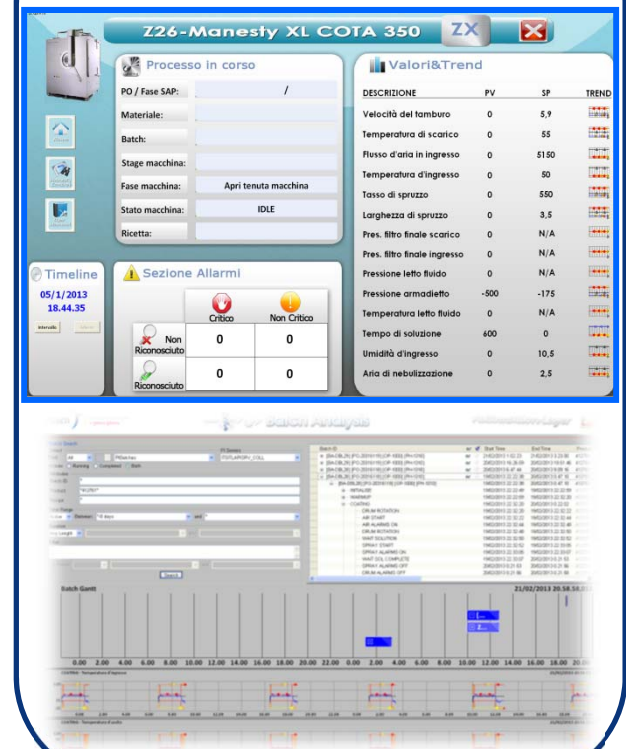
Content



Execution



Visualization



Manufacturing Process Operations

Product Lifecycle Management
Standards & Product Libraries

Orchestrated Execution

Quality Monitoring & Analysis



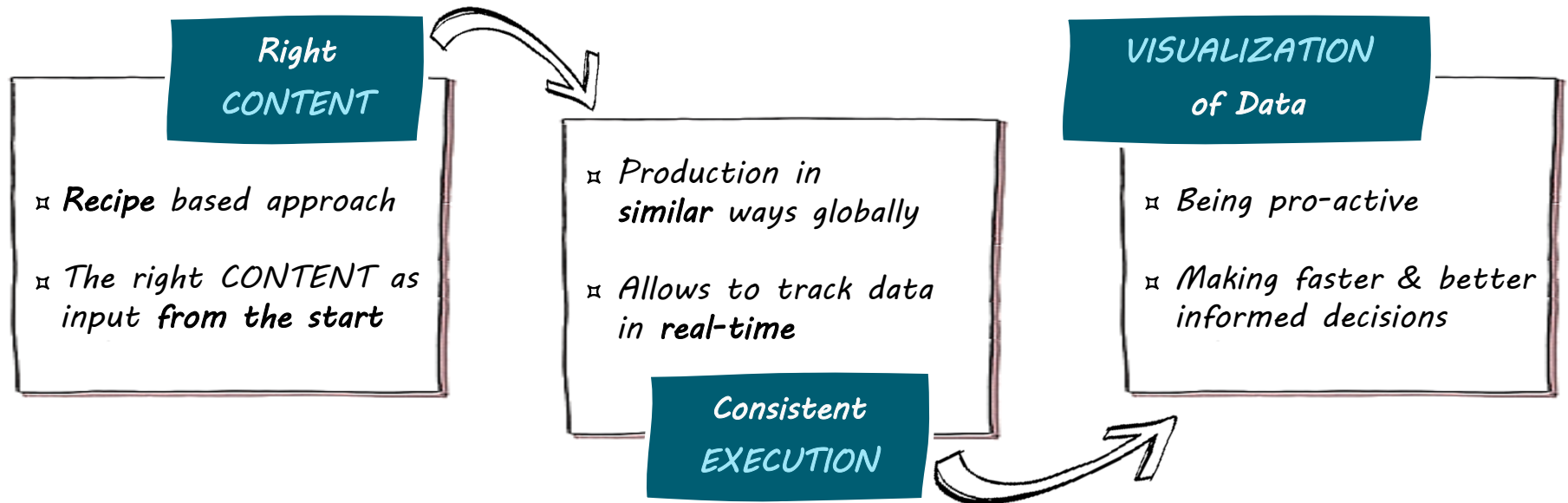
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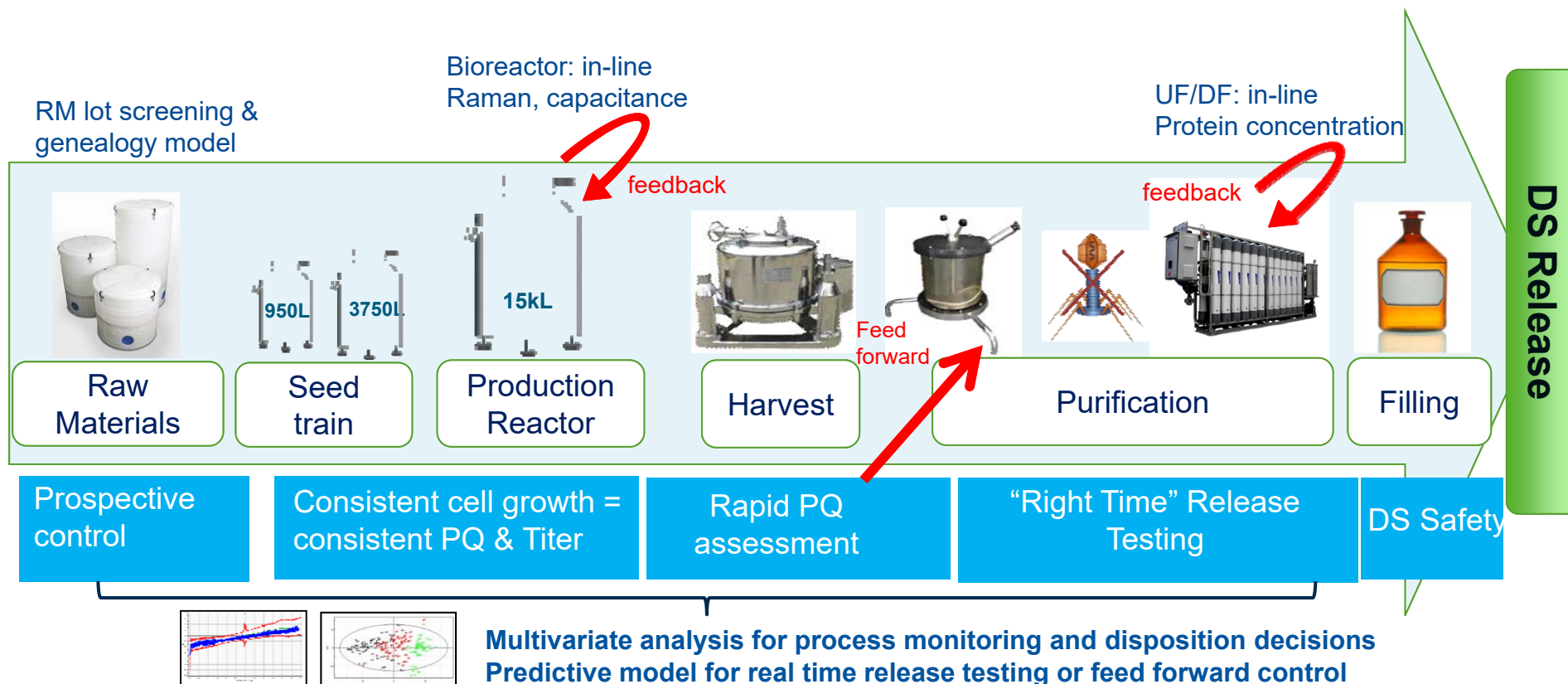
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Benefits of E2E Framework



- Reproducible execution enables quality review by exception
- Processes defined and orchestrated in a standard manner tied to regulatory filing
- Practiced on all manufacturing floors, laboratories and clinical sites
- Enabling integration of internal & external manufacturing
- Data Centric, not Document Centric

Advanced Process Control

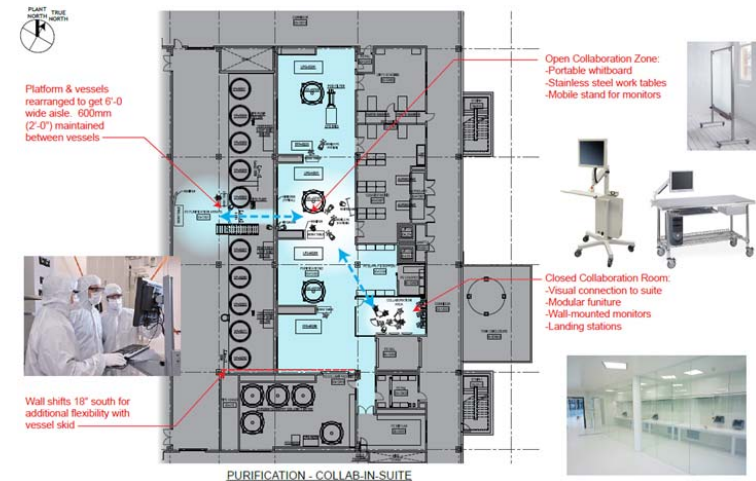
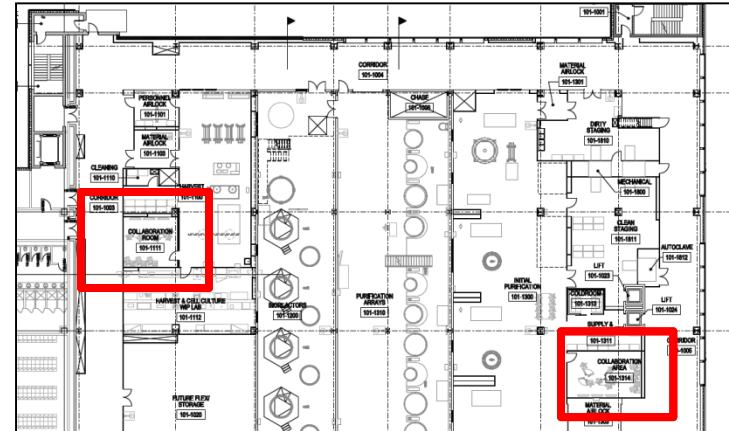


Foundations:

- Extensive RM, process, product characterization and understanding
- A fully-integrated control system

Integrated Work Environments

- 7 collaboration rooms / BMC
- Flexible Space
- Centrally located
- Adaptable furniture
- Visualization area for the process



PLANNED SUSTAINABLE FEATURES AT SOLOTHURN

83%
FEWER CARBON
EMISSIONS

79%
LESS ENERGY

89%
LESS WATER

Per kilogram of output based on Life Cycle Assessment results

HEAT RECOVERY SYSTEM

fed by chilled water heat recovery supplemented by solar power



ELECTRICITY
FROM WASTE-
TO-ENERGY

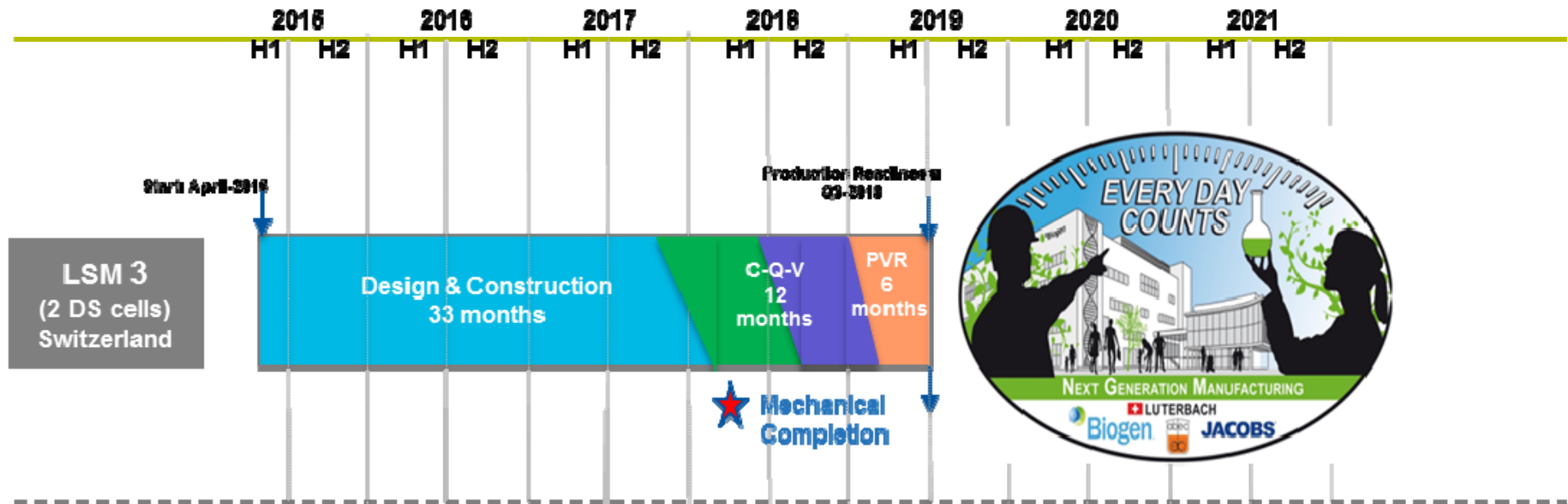
Remediation of
FORMER
BROWNFIELD
SITE

MODULAR
BUILDING
DESIGN
*for adding
future capacity*

Open manufacturing
environment with
NATURAL
LIGHTING

ERGONOMIC
DESIGN
*to promote employee
health and wellness*

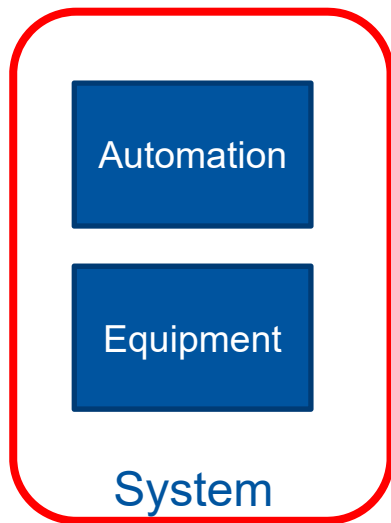
Aggressive Schedule



- 51 months from start to PVR complete
- 33 months for Design & Construction
- 12 months for CQV
- 6 months for PVR execution

System Validation Approach

Enhanced compliance through System Validation and Continuous Verification

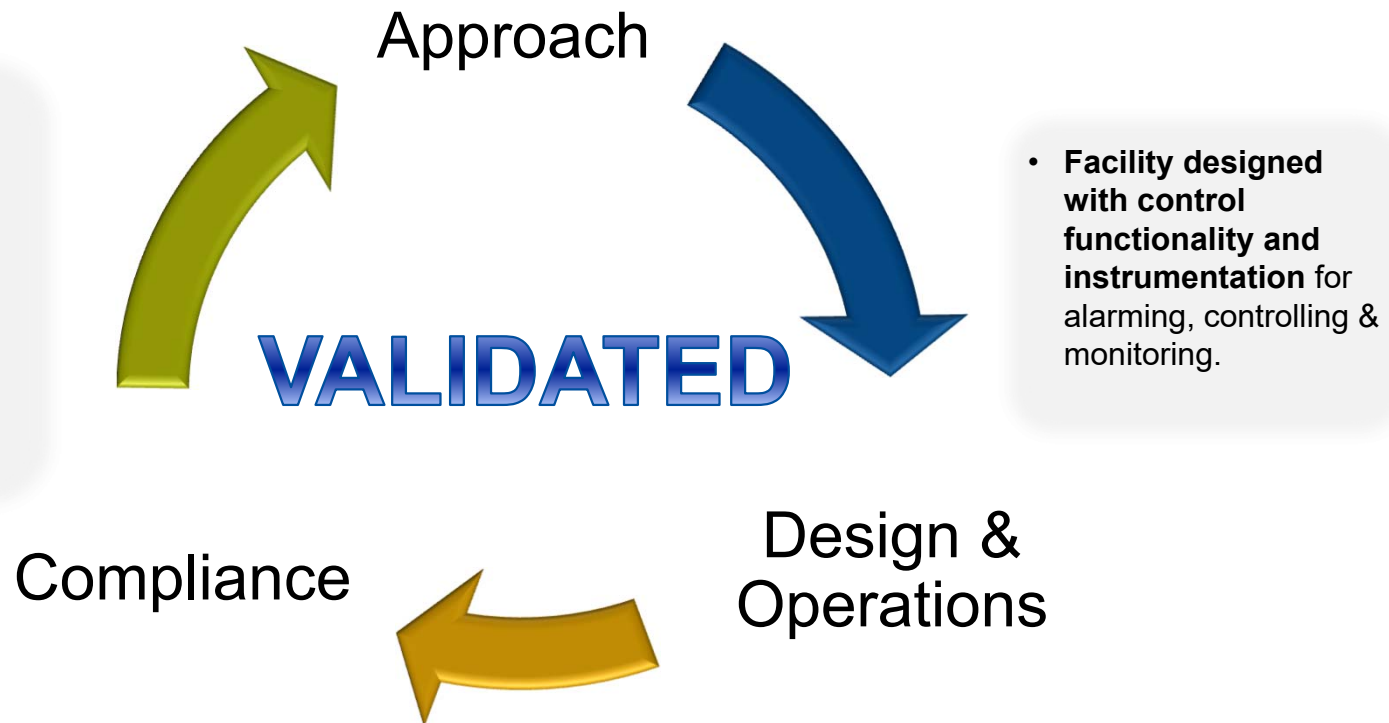


- System Validation – Equipment Class Approach
- Functional Specifications & Function Testing - Engineering Activities
- System Commissioning
- Global Library enables Recipe-Driven Operations
- Based on Continuous Verification approach

Continuous Verification

- **Automation Validation, Loop Checks, and Calibrations** are required for system functionality.
- **Historical OQ Validation is not required** – where functionality is real-time alarmed, controlled and monitored using validated automation systems.

- **Real-time verification** of key control functionality.
- **FMEA** to assess & mitigate risks.
- **Regulatory meetings:** Discuss proposed approach and level of risk



Enhanced compliance by demonstrating continuous state of control

Progress Report

- Detail design on track to complete Jan 2017
- Construction remains on accelerated milestone schedule
- Equipment fabrication on schedule, 1st FAT performed in Sep 2016
- Project focus remains on creating a safe working environment
- Energize first utility system April 2017
- Process Equipment arrives on site Apr 2017
- Integrated Commissioning and Validation starts Q4 2017
- Mechanical complete first BMC Q1 2018



Next Generation Manufacturing Goals

PROJECT PURPOSE

Provide our patients
meaningful therapies by 2020

PROJECT MISSION

Every day counts. Every day we will:

- Make an **Impact**
- Go home **Healthy**
- **Transform** lives

We act as if a million patients are counting on us to perform today.
Because they are!



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Acknowledgements

Biogen Project Team
Jacobs Engineering
CRB Engineers
ABEC



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INSERT HERE YOUR COMMENTS/QUESTIONS

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